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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,907	06/29/2007	Heike Gielen-Haertwig	BHC 04 1035	1084

35969 7590 10/27/2009

Barbara A. Shimei
Director, Patents & Licensing
Bayer HealthCare LLC - Pharmaceuticals
555 White Plains Road, Third Floor
Tarrytown, NY 10591

EXAMINER
BERNHARDT, EMILY B

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,907	GIELEN-HAERTWIG ET AL.	
	Examiner	Art Unit	
	EMILY BERNHARDT	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/06 & 4/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The abstract of the disclosure is objected to because it does not depict a structural formula describing the invention. Correction is required. See MPEP § 608.01(b).

Claim 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The R^6 scope is not consistently presented. The format begins “a group of the formula” followed by a “ * “ and then the structure. However on p.70 it appears dialkylaminocarbonyl is a choice for R^6 as there are species in the specification with this choice but it is presented in the format used for substituents on R^6. See also on p.71 which recites 3 additional aminocarbonyl choices which could be construed as choices for R^{6E} . This appears also in claim 2-4 and is embraced in the remaining claims.

2. If claim 12 is intended to be an independent claim it must completely identify all variables being claimed within the claim.

3. In claim 13 routes (A) and (B) it should be made clear what is being made since applicants are claiming alternate formulas as final products. Also in route (C) “such as “ renders the scope uncertain since its not clear what is being claimed-subject matter before or after the term.

4. Claim 15 is not further limiting the scope of claim 14 since intended uses in such claims are given no material weight. Note In re Tuominen 213 USPQ 89.

5. Claims 17-19 provides for the use of compounds, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 17-19 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 12-20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can only refer back to previous claims in the **alternative**. See MPEP § 608.01(n).

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for free base and salt forms, does not reasonably provide enablement for hydrate/solvate forms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and thus use the invention commensurate in scope with these claims. There is no process enabling such a scope in the specification . Note Vippagunta provided in herein who flatly states on p.18, section 3.4 the following: “Predicting the formation of solvates or hydrates of a compound…. is complex and difficult.” Applicants' own specification confirms this since despite numerous examples presented none of the compounds were obtained as solvates. Pursuant to In re Wands, 8 USPQ2d 1400, factors such as 1)

direction or guidance- none is seen in the specification as to what solvent would be suitable except for water;

2) presence or absence of working examples- there is none in the present case; 3) breadth of the claims- scope is easily in the millions; and 4) quantity of experimentation needed to make or use the invention must be considered to determine if undue experimentation is present. With regard to quantity of experimentation needed,it would be enormous given compounds of the instant scope would need to be synthesized and then exhaustively crystallized from the gamut of solvents reported to form solvates in the literature, followed by an examination of the crystal structure to see if any solvate has formed.

Claims 1-3 and 5-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the scope embraced by claim 4, does not reasonably provide enablement for remaining generic scope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Scope of substituted dihydropyridones being claimed is not adequately enabled. An assortment of rings can be present on the 1- and 4-positions as well as hetero rings as substituents in R4,R6 choices . From a reading of the specification on p. 9-10 heteroaryl and heterocyclyl can include up to 4 hetero atoms in any array and degree of unsaturation and also includes bicyclo ring systems.

Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made

much less tested showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the billions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature involving inhibitory activity as HNE inhibitors. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- as stated above the compounds actually made and tested represent a tiny fraction of what is claimed;

4) State of the prior art- The compounds are dihydropyridones which require aromatic rings at both the 1- and 4-position with varying substitution throughout the remaining ring . While compounds having the basic structure are known for the same activity as evident by the art cited by the examiner, they are likewise exemplary of similarly substituted groups at remaining ring positions as herein;

5) Working examples- While test data has been presented it is directed to a very small number of compounds (i.e.10) with a statement that remaining prepared compounds which are representative of claim 4 not claim 1 show an IC50 range that is

100-fold and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-11 and 13-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Gielen (WO'410). The commonly assigned publication has a different inventive entity than herein and an international filing date that precedes applicants' foreign priority date. Gielen describes compounds within the instant scope for the same activity and uses as claimed herein and also describes the same processes of making. See examples 34 and 99.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gielen (WO'210). While the subject matter of claim 12 is not anticipated it is rendered obvious by the teachings of Gielen who teaches in addition to alkoxycarbonyl and cyano, acetyl as a choice at instant R4/ See example 45in Gielen which is an example of such. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to modify the anticipated compounds in Gielen pointed out in the above 102 rejection by replacing the ester or cyano group with acetyl and in so doing obtain additional compounds for the same activity/uses taught by the art in view of the equivalency teaching outlined above.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3,5-10,12-17 of U.S. Patent No. 7,230,017. Although the conflicting claims are not identical, they are not patentably distinct from each other because they embrace overlapping subject matter. Note that all the variables overlap to a large degree. While R^6 do not completely overlap there is common subject matter when R^6 can be pyrollidinocarbonyl . Note that the species eg.34 in the US patent reads on the instant scope. US'017 corresponds to WO'410 applied above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 7,230,017, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Bernhardt/
Primary Examiner, Art Unit 1624